

# PATENT SPECIFICATION

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**International Classification:**—C07c. A61k, I. C11d. D06m.

## COMPLETE SPECIFICATION

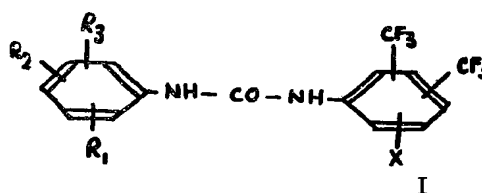
### New Diphenyl Urea Derivatives, processes for their production and Compositions containing same

5 We, J. R. GEIGY A.-G. a body corporate organised according to the laws of Switzerland, of 215, Schwarzwaldallee, Basle, Switzerland, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

10 The present invention concerns a process for the production of new insecticidal and bactericidal derivatives of diphenyl urea which have an affinity to keratin fibres in aqueous dispersion and which protect the treated keratin material from attack and injury by larvae of microlepidoptera (such as moths) and certain species of beetle (such as fur and carpet beetles). The invention also concerns the diphenyl urea derivatives obtained by the production process as well as the pest control agents containing these new compounds as active substances and the use of the new compounds for pest control, in particular for the protection of keratin material from injury by insects and also the keratin material protected in this way from injurious insects. In addition, the invention also concerns disinfectants and disinfectant cleansing agents, in particular textile washing agents and toilet soaps, which contain the new active substances as well as the use of these agents for the disinfection or simultaneous cleansing and disinfection of objects of all types, in particular also of fabrics containing cellulose.

35 It is known that halogenated diphenyl ureas have antibacterial and insecticidal properties which are particularly marked if there is a  $\text{CF}_3$  group in the molecule.

40 It has now surprisingly been found that substituted diphenyl urea derivatives having two  $\text{CF}_3$  groups in one benzene nucleus, of the general formula



wherein  $R_1$  represents hydrogen, a halogen atom, the trifluoromethyl group or the nitro group. 45  
 $R_2$  represents hydrogen, a halogen atom, the trifluoromethyl group or an alkyl or alkoxy radical having from 1 to 5 carbon atoms. 50  
 $R_3$  represents hydrogen, a halogen atom or a phenoxy or phenylmercapto radical possibly substituted by one or more chlorine atoms or alkyl groups having from 1 to 5 carbon atoms, and 55  
X represents hydrogen, a halogen atom or an alkoxy group having from 1 to 5 carbon atoms, 60

65 have considerably better insecticidal activity, in particular against insects, in all stages of their development, which are injurious to keratin material such as moth larvae, fur and carpet beetle larvae and, in addition, are suitable, because of their better bactericidal activity, as disinfectant and antibacterial active ingredients for the production of disinfectants and also of disinfectant washing and cleansing agents. In the general formula I, the two  $\text{CF}_3$  groups are advantageously in the meta position with regard to each other, in particular in the 3- and 5-positions of the benzene nucleus. 70

The new diphenyl urea derivatives of the general formula I are produced according to

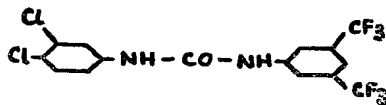


which contain a higher molecular aliphatic or alicyclic hydrocarbon radical as ring substituent. On stirring such preparations in aqueous treatment liquors, milky dispersions are obtained, from which the diphenyl urea derivatives according to the invention are fixed fast to washing, milling, light and dry cleaning onto keratin fibres, in particular wool, in the warm. Keratin fibres treated in this way with a content of at least 0.1 to 0.5% of active substance are durably protected from injury by larvae of microlepidoptera and certain types of beetle.

Compared with the known, halogenated diphenyl ureas or those containing  $\text{CF}_3$  groups, the new compounds having two  $\text{CF}_3$  groups in the same benzene ring have the advantage of considerably greater activity, particularly against the injurious larvae of *Attagenus* and *Anthrenus* species.

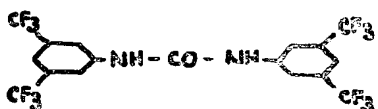
The following examples illustrate the production process according to the invention. Parts are given therein as parts by weight and the temperatures are in degrees Centigrade.

## EXAMPLE 1



229 Parts of 3,5 - bis - (trifluoromethyl) - aniline are added to a solution of 188 parts of 3,4 - dichlorophenyl isocyanate (produced by known methods from 3,4 - dichloraniline and phosgene, see, for example, W. Siefken, *Annalen der Chemie*, 562, 96—136, (1948)) in 1000 parts of nitrobenzene. The reaction mixture is heated for 3 hours at  $80^\circ$ . On cooling, the greater part of the diphenyl urea derivative precipitates. It is filtered off under suction and further purified by recrystallisation from methanol. The pure 3,5 - bis - (trifluoromethyl) - 3',4' - dichloro - N,N' - diphenyl urea melts at  $210\text{--}212^\circ$ .

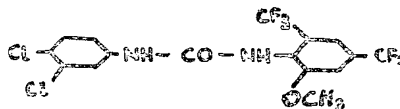
## EXAMPLE 2



229 Parts of 3,5 - bis - (trifluoromethyl) - aniline are dissolved in 800 parts of acetone. Phosgene is introduced into this solution at  $35\text{--}40^\circ$  and at the same time a solution of 190 parts of sodium acetate in 500 parts of

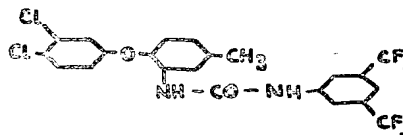
water is added dropwise. Phosgene is introduced until the solution just becomes weakly acid. The reaction mixture is then diluted with water and the precipitate which forms is filtered off under suction. After washing with water it is recrystallised from methanol. The melting point of the pure 3,5,3',5' - tetra - (trifluoromethyl) - N,N' - diphenyl urea is  $242\text{--}243^\circ$ .

## EXAMPLE 3



259 Parts of 2 - methoxy - 4,6 - bis - (trifluoromethyl) - aniline are dissolved in 600 parts of chlorobenzene and 188 parts of 3,4 - dichlorophenyl isocyanate are added to this solution dropwise at  $60^\circ$ . The reaction mixture is kept for 4 hours at  $60\text{--}65^\circ$  and then cooled whereupon the greater part of the reaction product precipitates in crystalline form. It is filtered off under suction and, in the crude form, melts at  $200\text{--}210^\circ$ . The pure compound is obtained by recrystallising twice, first from chlorobenzene and then from isopropanol. It then melts at  $220\text{--}222^\circ$ .

## EXAMPLE 4

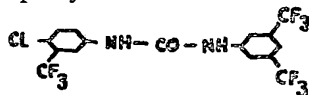


A solution of 252 parts of 3,5 - bis - (trifluoromethyl) - phenyl isocyanate in 2000 parts of chlorobenzene is added dropwise to a previously prepared solution of 278 parts of 2 - amino - 4 - methyl - 3',4' - dichlorodiphenyl ether in 1000 parts of benzene. The mixture is heated for 6 hours at  $80\text{--}85^\circ$ . After cooling, the crude product is filtered off under suction and, after drying in vacuo, it melts at about  $180^\circ$ . The compound is purified by recrystallising twice from chlorobenzene and then melts at  $190\text{--}192^\circ$ .

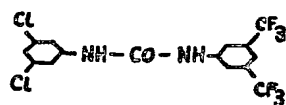
The following compounds can be produced as described in the previous examples from carbonic acid derivatives, and corresponding starting materials of formula II or their isocyanates, and 3,5 - bis - (trifluoromethyl) - aniline; wool treated with these compounds is protected from injury by the larvae of moths, fur and carpet beetles.

diphenyl urea derivative

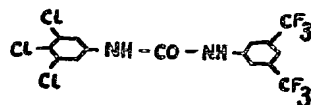
M.P.



164-166°

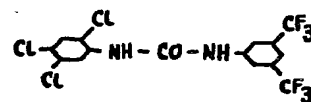


212-214°

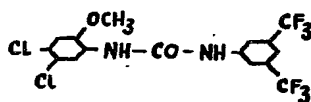


318-321°

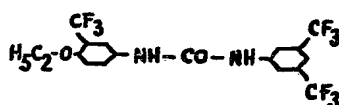
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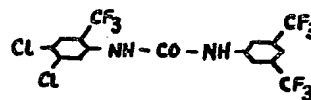
280-283°



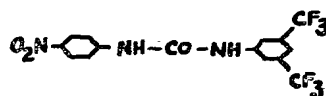
190-193°



203-205°

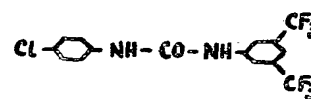


194-197°

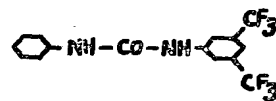


289-293°

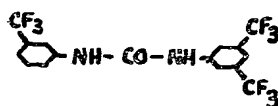
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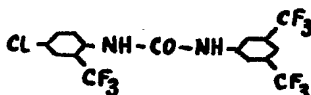
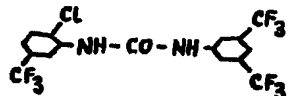
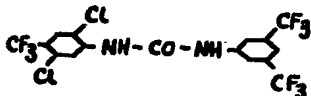
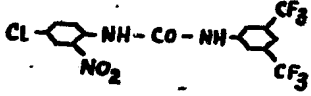
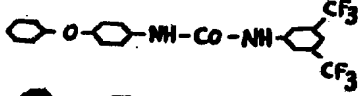
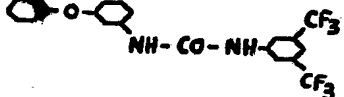
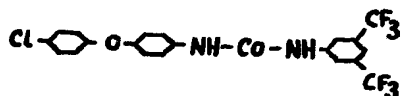
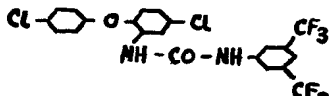
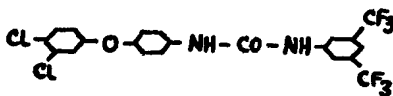
212-213°



183-184°



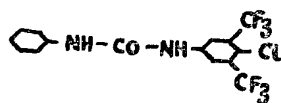
172-173°

	diphenyl urea derivative	M.P.
		202-203°
		208-210°
		190-192°
5		184-186°
		171-172°
		176-177°
		181-183°
		196-198°
10		188-190°

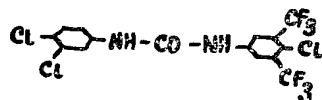
	diphenyl urea derivative	M.P.
		182-185°
		189-191°
		199-200°
5		190-192°
		183-185°
		179-180°
		190-191°
		180-182°
10		178-180°
		186-188°
		182-183°
		188-190°
		217-218.5°

15 On choosing 3,5 - bis - (trifluoromethyl) - 4 - chloraniline as starting material of the formula III, the following compounds can be produced in a similar manner:

M.P.



185-191°



223-225°

5 The diphenyl urea derivatives of formula I  
 10 produced by the process described have con-  
 siderable affinity to keratin material and are  
 15 excellently suitable, therefore, for the protec-  
 tion of keratin material from injury by insects,  
 particularly for the fast-to-washing mothproof-  
 20 ing of such types of materials, both in the  
 raw and processed state, e.g. of raw or pro-  
 cesses wool as well as other animal hairs, fells  
 and furs. In addition, these compounds can  
 be employed for the impregnation of wool and  
 25 woollen articles whereby excellent mothproof-  
 ing is also attained.

Apart from their insecticidal activity against  
 the larvae of the clothes moth, the compounds  
 of formula I also have such action against the  
 30 larvae of the fur and carpet beetles that keratin  
 materials such as blankets, woollen carpets,  
 woollen underwear, woollen clothes and knitted  
 goods treated with the compounds according  
 to the invention are protected against all types  
 35 of injurious insects.

An example is given below of the applica-  
 tion of the new active ingredients.

#### EXAMPLE 5

30 0.2 Parts of the compound according to  
 example 1 are dissolved in 5 parts of glycol  
 monomethyl ether. 5 Parts of sulphonated  
 castor oil are added to this solution which is  
 then diluted to 6000 parts by volume with  
 35 water. 200 Parts of wool are introduced into  
 the cold dispersion obtained and it is then  
 slowly brought to the boil, and finally boiled  
 for one hour. After rinsing and drying in the  
 usual way, the wool so treated proves to be  
 40 completely resistant to attack by the larvae  
 of moths and *Attagenus* and *Anthrenus* species.

Apart from the insecticidal activity, the com-  
 pounds of formula I according to the invention  
 have also a very good bactericidal action.

45 For most purposes for which antibacterial  
 active substances are used for disinfection,  
 whether for the purpose of simultaneous cleans-  
 ing or only for disinfection itself, it is import-  
 ant that the active substances retain their  
 50 activity in the presence of capillary active  
 substances. This is the case with the com-  
 pounds used according to the invention as  
 active substances so that they are excellently

suitable for incorporation into disinfectant  
 washing and cleansing agents as well as into  
 disinfectants which in their composition also  
 55 contain capillary active substances which do  
 not serve the purpose of cleansing, for ex-  
 ample emulsifying and dispersing agents.

For the production of disinfectant washing  
 and cleansing agents, the active substances of  
 general formula I used according to the inven-  
 60 tion are incorporated in a finely distributed  
 form or possibly dissolved in organic solvents  
 into the cleansing agents which have possibly  
 been kept in a liquid condition. In particular,  
 65 capillary active substances of an anion active  
 type such as alkali metal soaps or ammonium  
 soaps of fatty acids having from 10 to 20  
 carbon atoms, salts of alkyl sulphuric acids or  
 of aliphatic or aromatic sulphonic acids;  
 70 cation active substances such as quaternary  
 ammonium compounds having at least one  
 aliphatic or araliphatic radical, the aliphatic  
 portions of which contain from 10 to 20  
 carbon atoms, as well as non-ionogenic sub-  
 75 stances such as the condensation products of  
 ethylene oxide with alkanols having from 10  
 to 20 carbon atoms, with alkyl phenols or with  
 partial fatty acid esters of polyhydroxy com-  
 80 pounds such as, e.g. sorbitan, are used as  
 washing and cleansing agents.

Agents which are only intended for dis-  
 infectant purposes can be solutions, suspen-  
 sions or emulsions which, apart from the  
 active substances used according to the inven-  
 85 tion, possibly also contain capillary active  
 substances, for example of the type given  
 above. Preparations of semi-solid, ointment-  
 like consistency can also be used as disinfect-  
 90 ants. Disinfectants according to the invention  
 can be applied by painting or spraying the  
 objects to be disinfected with the preparation  
 concerned. It is also sometimes possible to  
 dip the objects into the preparation.

95 Contents of a few percent of active sub-  
 stances used according to the invention in the  
 disinfectant, washing or cleansing agents, and  
 of fractions of percentages in the disinfectant  
 application liquors possibly used for simult-  
 100 aneous cleansing, are sufficient to attain effec-  
 tive disinfection.

It was not to have been expected that the active substances used according to the invention would retain their antibacterial activity in the presence of capillary active substances, in particular in the presence of the alkali metal soaps of higher fatty acids which are the most important components of washing agents. The active substances used also have good fastness to light so that they cause practically no yellowing in soaps.

Apart from the active substances, the soaps or other washing and cleansing agents can contain the usual fillers such as alkali sulphates, carbonates or phosphates as well as the other additives usual in cleansing agents.

The disinfectant cleansing agents according to the present invention can be put to the most various uses. For example, they can be used in human and veterinary hygiene for cleansing and simultaneous protection against bacteria causing diseases either direct on the skin or via the mouth or causing perspiration odours. Examples of such infective bacteria are *Staphylococcus aureus*, *Escherichia coli*, *Sarcina lutea* and *Sarcina alba*, and of those decomposing perspiration are *Proteus vulgaris*, *Bacillus mesentericus* and *Bacillus subtilis*. In such cases, the most usual cleansing agent components are soaps, but also, according to the present invention, the antibacterial active ingredients defined above can also be combined with cosmetics such as ointments, creams or skin lotions which contain other capillary active substances, for example in the form of dispersing agents.

Naturally, disinfectants can also be produced which, in addition to the active substances according to the present invention, contain other active ingredients which are suitable for increasing or modifying the action.

Disinfectant cleansing agents according to the present invention can also be used, for example, for the cleansing of textiles or leather; the ready-for-use soaking, washing, cleansing and rinsing liquors to which the antibacterial active ingredients have been added later, i.e. after dissolving the capillary active substances in water, also being washing and cleansing agents according to the present invention. Like the use thereof, they also fall within the scope of the present invention. Also, the substituted diphenyl ureas of the general formula I can be combined with dry cleaning agents, i.e. dissolved in aliphatic or aromatic, possibly chlorinated, hydrocarbons, most of which generally also contain capillary active wetting and cleansing agents which are soluble in oil.

Finally, the antibacterial cleansing agents according to the present invention can be used also for the disinfection of other organic or inorganic objects. Thus, they are valuable, for example, for the antibacterial cleansing of apparatus and objects in hospitals such as surgical instruments, instrument tables, vessels, and laboratory utensils, as well as of equip-

ment and vessels in food and fermentation industries.

Preferred active ingredients of general formula I are 3,5 - bis - (trifluoromethyl) - 3',4' - dichloro - N,N<sup>1</sup> - diphenyl urea and 3,5 - bis - (trifluoromethyl) - 4' - chloro - N,N<sup>1</sup> - diphenyl urea.

The following examples illustrate the production of the disinfectants and disinfectant cleansing agents according to the invention as well as the use of these agents. Parts are given therein as parts by weight and the temperatures are in degrees Centigrade.

#### EXAMPLE 6

75 Parts of coconut oil (saponification number 262) and 25 parts of castor oil (saponification number 175) are saponified at 115° with 120 parts of an about 15% sodium hydroxide solution. 3 Parts of 3,5 - bis - (trifluoromethyl) - 3',4' - dichloro - N,N<sup>1</sup> - diphenyl urea or 3,5 - bis - (trifluoromethyl) - 3',5' - dichloro - N,N<sup>1</sup> - diphenyl urea are then added to the still liquid soap and the mixture is homogenised well. After salting out, the soap is poured into moulds and allowed to cool. Pieces of household soap are obtained which, on being used for washing, are characterised by a good antibacterial action.

#### EXAMPLE 7

To produce an antibacterial toilet soap, 98 parts of soda soap filings are well mixed with 2 parts of 3,5 - bis - (trifluoromethyl) - 4' - chloro - N,N<sup>1</sup> - diphenyl urea. The mixture is then milled and pressed into the usual moulds.

#### EXAMPLE 8

A combination of 2 parts of 3,5 - bis - (trifluoromethyl) - 4' - chloro - N,N<sup>1</sup> - diphenyl urea with 25 parts of triethanolamine salt of n-dodecyl sulphuric acid, 1 part of n-dodecyl alcohol, 3 parts of triethanolamine sulphate, 1 part of lauric acid mono-glyceride and 68 parts of water can be used as a liquid toilet soap and also as shampoo. It has a good antibacterial action.

#### EXAMPLE 9

5 Parts of 3,5,3' - tri - (trifluoromethyl) - 4' - chloro - N,N<sup>1</sup> - diphenyl urea, 7 parts of a non-ionogenic washing agent (obtained by condensing 2,4-diamyl phenol with 10—12 mols of ethylene oxide), 30 parts of sodium metasilicate and 58 parts of tetra-sodium pyrophosphate are well mixed together whereupon a cleansing agent having antibacterial properties is obtained. A 1% aqueous solution of this agent is excellently suitable as a disinfectant washing liquor for the cleansing of linen, clothes, crockery and other objects.

#### EXAMPLE 10

A disinfectant dry cleaning agent is obtained by dissolving 0.5 parts of 3,5,3',5' - tetra - (trifluoromethyl) - N,N<sup>1</sup> - diphenyl urea and 5 parts of a condensation product of nonyl phenol with 15 mols of ethylene oxide in 94.5 parts of tetrachloroethane or the same amount of trichloroethylene.

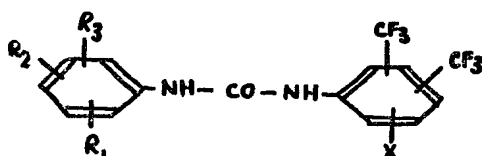


## EXAMPLE 11

An antibacterial skin cream is obtained by thoroughly mixing the following components: 13 parts of glycol monostearate, 1 part of sodium dodecyl sulphate, 2 parts of polyethylene glycol 1500, 3 parts of wax, 3 parts of viscous paraffin oil, 2 parts of wool fat, 3 parts of polyoxyethylene sorbitan mono-oleate, 6 parts of glycerine, 0.1 parts of perfume, 0.1 parts of p-hydroxybenzoic acid methylester, 2 parts of 3,5 bis - (trifluoromethyl) - 3<sup>1</sup>,4<sup>1</sup> - dichloro - N<sub>2</sub>N<sup>1</sup> - diphenyl urea. Instead of 3,5 - bis - (trifluoromethyl) - 3<sup>1</sup>,4<sup>1</sup> - dichloro - N<sub>2</sub>N<sup>1</sup> - diphenyl urea, also 3,5 - bis - (trifluoromethyl) - 4<sup>1</sup> - chlorodiphenyl urea can be used.

## WHAT WE CLAIM IS:—

1. Process for the production of insecticidally and bactericidally active derivatives of diphenyl urea of the general formula



I

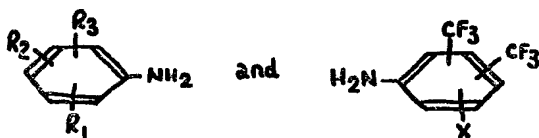
wherein R<sub>1</sub> represents hydrogen, a halogen atom, the trifluoromethyl group or the nitro group,

R<sub>2</sub> represents hydrogen, a halogen atom, the trifluoromethyl group or an alkyl or alkoxy radical having from 1 to 5 carbon atoms,

R<sub>3</sub> represents hydrogen, a halogen atom or a phenoxy or phenylmercapto radical possibly substituted by one or more chlorine atoms or alkyl groups having from 1 to 5 carbon atoms,

X represents hydrogen, a halogen atom or an alkoxy group having from 1 to 5 carbon atoms,

which comprises reacting by known methods, possibly in steps and in any order desired, one mol of a reactive derivative of carbonic acid with one mol of each of two aminobenzene compounds of the general formulae



II

III

wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and X have the meanings given above.

2. Process according to claim 1 for the production of 3,5 - bis - (trifluoromethyl) - di-

phenyl urea derivatives, which comprises using a 3,5 - bis - (trifluoromethyl) - aniline possibly substituted by a halogen atom, as starting material of the general formula III.

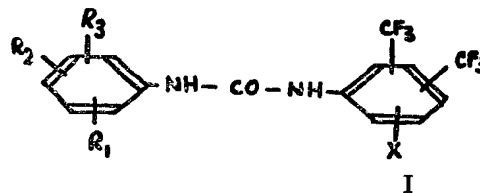
3. Process according to claim 1 for the production of symmetrically substituted diphenyl urea derivatives which comprises reacting 1 mol of a reactive derivative of carbonic acid, in particular phosgene, with 2 mols of a compound of the general formula III given in claim 1.

4. Process for the protection of keratin material from injurious insects, which comprises treating the material with agents which contain diphenyl urea derivatives of the general formula I given in claim 1.

5. Agents for the protection of keratin material from injurious insects, characterised by a content of diphenyl urea derivatives of the general formula I given in claim 1, such derivatives being in a finely distributed form, possibly combined with suitable carriers or solvents and/or distributing agents.

6. The keratin material protected from injurious insects by the use of compounds of the general formula I.

7. Diphenyl urea derivatives of the general formula



I

wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and X have the meanings given in claim 1.

8. The manufacture of a disinfectant and disinfectant cleansing agent wherein at least one bacterial diphenyl urea derivative of the general formula I given in claim 1 is mixed with a capillary active agent.

9. A disinfectant and disinfectant cleansing agent comprising as active ingredients at least one bactericidal diphenyl urea derivative of the general formula I given in claim 1 and a capillary active agent, especially a cleansing agent.

10. A disinfectant and disinfectant cleansing agent according to claim 9 wherein the active ingredient is 3,5 - bis - (trifluoromethyl) - 3<sup>1</sup>,4<sup>1</sup> - dichloro - N<sub>2</sub>N<sup>1</sup> - diphenyl urea.

11. A disinfectant and disinfectant cleansing agent according to claim 9 wherein the active ingredient is 3,5 - bis - (trifluoromethyl) - 4<sup>1</sup> - chloro - N<sub>2</sub>N<sup>1</sup> - diphenyl urea.

12. A disinfectant and disinfectant cleansing agent according to claim 9 wherein the capillary active agent is an alkali metal soap of fatty acids having from 10 to 20 carbon atoms.

13. A process for the disinfection of inorganic and organic inanimate objects, in particular of cellulosic fabrics, which comprises applying to them a disinfectant and disinfectant cleansing agent according to claim 9 with a content of at least one diphenyl urea derivative of the general formula I as active ingredient.
14. A process as claimed in claim 1 in which  $R_3$  represents hydrogen, a halogen atom, or a phenoxy radical possibly substituted by one or more chlorine atoms.
15. Diphenyl urea derivatives as claimed in claim 7 in which  $R_3$  represents hydrogen, a halogen atom, or a phenoxy radical possibly substituted by one or more chlorine atoms.
16. A process as claimed in claim 1 substantially as hereinbefore described in any one of Examples 1 to 4.
17. A process as claimed in claim 14 substantially as hereinbefore described in any one of Examples 1 to 4.
18. Diphenyl urea derivatives as claimed in claim 7 substantially as hereinbefore described in any one of the Examples.
19. Diphenyl urea derivatives as claimed in claim 15 substantially as hereinbefore described in any one of the Examples.

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